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CONCERNING THE AMERICAN MATERIA MEDICA.*

By John Uri Lloyd, Phar.M., Cincinnati, Ohio.

PROLOGUE.

This subject cannot be considered, even superficially, by one who comprehends, even to a degree, its outreaches, without a question as to whether, by reason of the limitation of time, that which most appeals may be reached at all. Its field touches and its substance involves the various professions and arts of medicine, botany, chemistry, pharmacy, and biology in their many and diversified phases. But scant justice can be given to most of these, for they could not be satisfactorily treated in a volume.

The course of the American materia medica has been tortuous. In an historical sense its beginnings are all-important, and must neither be evaded nor neglected by me, even though, by reason of the time consumed in its telling, that which most I crave to say be left unsaid. I do not know that any one has ever before attempted to construct an orderly sequence of its story, nor do I know that any man has ventured, in a spirit of fairness, toleration, and admiration, to say a kind word for both friend and foe involved in the mazes of past prejudice and past action, in which so innocent a theme as the American materia medica served as a text. But this issue must be met by some man, some day. The facing of it to-day is not of my choice, but it is for me a duty. I shall therefore try, in the brief hour at my command, to do what is possible to connect

* Address delivered before the Philadelphia College of Pharmacy, November 4, 1909, being the third of a series of special lectures for 1909–10.

the past with the present. And in doing this, I shall draw not alone from what I have learned from print, but that which came from the lives of my associates, in whom I have been much blessed.

PART I.

CONCERNING PHILADELPHIA.—The pleasure of meeting one's friends amid such greetings as come when I visit this home of those whose work, past and present, has been in my own chosen field, is an inspiring ideal. But yet not without a degree of apprehension do I appear to-day in this institution, where it is my duty to consider discursively a subject which I shrink from attempting, even though it has taken my care and time for many decades. Well do I recall that twenty years ago I accepted in our neighboring city, New York, a like responsibility concerning a closely related subject, and at that time felt less hesitancy in attempting to discuss the "Infinities in Pharmacy," than I do now, concerning a subject on which I should, seemingly, be better informed. Let me not be misunderstood. The years of experience between then and now have been a teacher that bids me be cautious. As I now view the outreaches and intricacies of our text, the apparently more portentous one of other days is far overshadowed by that which lies within the title you have given me. Infinity, from whatever direction man's limitations meet the unknown, is incomprehensible; but no more superhuman text appears than lies within the subject awarded me to-day. This I claim to be able to demonstrate, if time and space permits me to reach the substance that rests beyond this introduction.

Need I, then, say that no one can better appreciate than do I the delicacy of the position I now occupy? Nor could any one appreciate more than do I the opportunities for error that lie in my path. Let me then be cautious, realizing, as I do, the responsibility and the complications, past and present, that I assume in touching a subject so closely connected with men's prejudices and antagonisms.

The historical surroundings of this spot take first my tenderest thought, and I crave a moment in their behalf. Am I wrong in accepting that this is the cradle in which was nourished the early American materia medica, as at that date the materia medica was known? While it is true that the Pilgrim Fathers, on the rocky coast of Massachusetts, began of necessity the investigation of a new flora in that New England land, it is also true that, creeping down the coast and across the lands and rivers intervening, the spirit

of research found here a place in which to rest, and from which to radiate. Credit for their achievements those who have achieved, be they who they may or where or when they lived, but yet concede that for a hundred years, during the burst of enthusiasm over the new land's productions, the greatest activity in the direction of my subject clustered about this spot.

In 1808 appeared, in Boston, the first Pharmacopœia of American physicians, but let us not forget that in the very building wherein I now speak, published in Philadelphia (1778), rests the only known copy of the first Pharmacopœia published authoritatively in America, under the auspices of the government of the United States. It emanated from Lancaster, almost a suburb of this city, and bore the official stamp of the embryonic nation. Could there have been a more precious book than this, issued in behalf of the struggling government? Since the publication of this epoch-marking book, a volume would be required were I even to attempt to record the titles or make a brief summary of the Philadelphia publications of world-wide celebrity on our subject.

As I think of those times and the records of the men who accomplished their mighty work in and about Philadelphia, the names of the participants that crush upon me stand second in importance to none in America. From this point the botanists Pursh and Nuttall pursued their explorations, and we all know the importance of their contributions to the study of the flora of North America. Here Dr. John Morgan became conspicuous, in that he was the first American physician to plead for the separation of the compounding of medicines from the process of medication, which, to use the words of Mr. Wilbert, he felt would be "commended in some directions, severely criticized in others."

In Philadelphia, about 1730, John Bartram established the first American botanical garden, and near here his cousin, Humphrey Marshall (1773), established the second. From the Jersey land near this point, Peter Smith began (1780) his travels down into and then through the southern country, thence back to Cincinnati, where (1812), under the title "Dispensatory," he printed the first medical book issued west of the Alleghenies. Need I call to your attention the two Bartons of one hundred years ago, and the work they accomplished, that of B. S. Barton (1798) being the first American attempt at a printed collection of the American materia medica, for that of Schoepf (1787) was issued in Germany? And

even in that foreign work, may not Philadelphia claim a full share of credit? For Schoepf was a Hessian soldier, who, on the surrender of Lord Cornwallis at a point relatively near where we now stand, travelled with pack on back from New York to Philadelphia, from which point he continued, even to Florida, searching the country throughout for materia medica specimens. But, as already stated, his descriptive book was, unfortunately for American records, written in a foreign tongue and printed (1787) in a foreign land. In this city the botanist preacher and pioneer Manasseh Cutler, of Massachusetts, received his doctor's degree and became a member of the celebrated Philosophical Society of Philadelphia, in the Proceedings of which (1785) appeared his "Vegetable Productions, Botanically Arranged." Here Dr. Benjamin Rush and a host of contemporary physicians served humanity's best interests, as they saw humanity's best interests under the limitations of that day. In Philadelphia was issued the rare publication, in two volumes (1828–1830), of that scholarly traveller, C. S. R. Rafinesque, whose scientific qualifications did so much to influence educational thought and action throughout the central west. I love to think of him as a professor in Transylvania University of Lexington, Kentucky, then the western centre of art, literature, and science, a colaborer with Audubon the bird painter of Louisville, Kentucky. To Philadelphia came that conspicuous searcher into America's materia medica, that antagonist to all forms of medication established "*by right of authority,*" Samuel Thomson, to discuss with Rush, Cutler, and Barton those things pertaining to medicine in his day. Here, under the auspices of the University of Pennsylvania and the Philadelphia medical societies, such researches were made as those of Downey, on sanguinaria (1803), and many other theses of like importance. Indeed, notwithstanding lost opportunities, the influence of the three great institutions, the University of Pennsylvania, Jefferson Medical College, and the Philadelphia College of Pharmacy, in such as this is world wide. Wherever in this land one touches life and activity in the direction of botany, pharmacy, medicine, materia medica, and allied subjects there flow their united currents.

To mention even briefly the records of the men no more among us, who come to mind as I review the work done in this great city, would take more time than can be devoted to the subject concerning which I shall speak. I must not attempt to name men yet living, nor yet can I presume to pass the more recent but not less important

efforts of such men as Wood, Bache, Procter, Maisch, Trimble, Parrish, and others whose faces, no longer with us, are to me as familiar as are those of the friends now about me. Nor yet can I neglect those concerned in establishing the great chemical industries of this city, Rosengarten, Powers, Weightman, Ellis, Bullock, Crenshaw, Carter, Scattergood, Bowers, and others. These, and such as these, have been mighty factors in our work, their names are inseparable from those of whom I have been speaking and are inseparably connected with American progress.

But, my friends, these reflections or reminiscences, bred by the subject awarded me, must be broken. Let me, however, hope that what I have said may lead my hearers to realize that in addressing this audience in this building I not only fully appreciate the honor conferred upon me but comprehend that in the face of these records of the past, in which so many men unnamed were also concerned, I have good reason to be apprehensive as to whether I can do justice to that past, and yet credit myself in aiming to serve my friends as I would like to do.

Early Conditions in Medicine.—Let us now revert to conditions pertaining to the day of those involved in the introduction of the early vegetable American materia medica. In those days, primitive men (and this term need not be restricted to the aborigines) were much closer to nature than is humanity at present. In addition to nature's contact, religious thought, or perhaps we may better say theological teachings, were more nearly hand in hand with man's opinions of life's objects than they are at present. Less disposed than now were men to question (aloud) the axiom (dogma) that the universe and all contained therein was formed for the sole purpose either of serving or of pestering mankind. Diseases were likewise more apt to be likened to organic entities, partaking much of the qualities of the self-conscious devils of old that, under the auspices of an allwise Creator, delighted in torturing mankind. Seemingly, but yet as a rule without defining or perhaps comprehending the subject in these words, disease was not considered as simply a departure from the normal, but as an invading entity that must be driven out by an antagonist more powerful but yet somewhat more friendly to the suffering person. Nor is this opinion of diseases altogether a thing of the past, nor are the aforenamed conceptions of primitive men wanting in some men of our day as regards precepts and concepts. The medicine-man of the Indians

was not alone in the belief in evil spirits or in devils that afflicted people with diseases that needs be conjured and potioned out. Nor is he yet deserted.

Let us not be surprised that at that date the trend of thought of many and the personal belief of not a few was to the effect that, in nature's store-house, ready for the use of man, were locked remedial agents antagonistic to every disease which sin-laden man had contracted or inherited. It was an oft-repeated maxim, that yet lingers, that God had placed in every country remedial agents to care for diseased mankind in that country. Nor is this, as already indicated, foreign to the belief of some to-day.

Let it not be accepted, however, that all men at that date were imbued with or even tinctured by this theological inheritance or professional conception. On the contrary, many talented investigators of what was known then as materia medica looked upon disease, as well as upon remedial agents, in quite a different manner. They believed, it is true, that nature possessed secret wealths that could be utilized by man for man's benefit (often through torture of the flesh), but which, yet, were no more *created* for man than that man was created for the purpose of being attacked by diseases or persecuted by evil spirits.

Thus came into play in the incipiency of the early American materia medica a blending of the intensely religious, the professionally dogmatic, and the hopefully scientific, as well as the ever-present commercially ambitious, all seeking alike the secrets that reposed in the natural products of the new world.

And yet another vital factor in the primitive development of the American materia medica must not be overlooked. In those days, authoritative remedial agents of European pharmacy were difficult to obtain. This necessitated the discovery of agents that would parallel the action of the old-time remedies. Emetics, cathartics, vesicants, anthelmintics, and such were seemingly as necessary to man's existence as food. The pioneers were versed in domestic medicine, and many were familiar with European works on the subject. They felt compelled to seek for substances possessed of qualities similar to those commended by such authors as Lewis, Culpepper, and Quincy.[1] Nor was this all. The marvellous stories

[1] Selecting therefrom too often the substances that produced systemic shock. Let it not be forgotten that the European herbalists attempted to utilize about every plant that grew.

told by the new world *promoters* concerning the fabulous wealth of soil and flora of the new-found land, the almost superhuman qualities imputed to some of the products by the advertising real-estate promulgators, fired the European mind and prepared settlers for almost any materia medica surprise. Witness, even in the days so near us as those immediately preceding the Revolution, the exaggerations concerning the Kentucky land, whose story was so graphically told in John Filson's "History of Kentucky." Witness also the marvellous record of cinchona (*Jesuit bark*) from South America, and of *sassafras* from "the Floridas." Think of the sensational introduction into Europe of tobacco, and the new foods, Indian corn and the potato. Comprehending all this and such as this, one may be in a position to realize the speculative importance to a half-clothed, suffering, needy, transplanted people, on the fringe of an undeveloped continent, of the blessings that might lie within an unknown flora, boundless in extent.

That was a day of heroics in therapy, and under the influence of tradition and environment substances most likely to gain a receptive hearing were such as strongly appealed to the senses by reason of their aromatic, emetic, cathartic, or other energetic qualities. Sassafras, serpentaria, senega, podophyllum, spigelia, and such, from North America, ipecac from the eastern coast of South America, cinchona and jalap from the land of the Incas, and such substances as hydrastis and sanguinaria, used by the Indians as pigments by reason of the fact that they both possessed bright colors and their juices were distasteful to pestering insects, may thus be cited.

With these thoughts in mind, let us now refer to Barton's "Collections," published in Philadelphia in 1798. Note the discreet sentence in the *Introduction*, indicating the fact that Dr. Barton comprehended the delicacy of his position as concerns both the people and the profession, for in those days, as already indicated, the people were deeply interested in materia medica subjects and were preparing to rebel against transplanted, mediæval European processes employed by the regular profession. This is apprehended by Barton, as follows:

> The readers of these "Collections" (for everything that is written and published solicits some readers) will form different opinions about my medical faith. Some of them will think I have too much; and others, that I have not enough.

Comes then the question as to what should be a part of the materia medica, concerning which the doctor asks a question as pertinent now as it was then, to wit,

> How are we to know what plants are most proper for the purposes of medicine, until we shall have examined the properties of a great body of vegetables?

Then comes a plea for toleration by his professional brethren:

> I wish to turn the attention of our physicians to an investigation of the properties of their native productions. When it is considered how little has hitherto been done in this way, every attempt (mine is an humble one) should be candidly received.

Next, in a cautious criticism, he applies himself directly to physicians, informing them that little had been done in the direction of the investigation of the American materia medica.

Skim now the substances suggested by Barton as being worthy of examination and their sources. Note that he credits alike Indian, pioneer, traveller, botanist, farmer, attorney, and statesman, mentioning Thomas Jefferson, then President of the United States, as commending a treatment to overcome a disease then prevalent in Virginia. But seldom does he credit a member of the medical profession as having done anything whatever! Note more specifically the importance given to energetic drugs, both those experimented with and those that were promising by reason of their relationship, botanically, to poisonous remedies in use. A few are kindly in their action, as, for example, cornus florida, boneset, and uva ursi, the *majority,* however, being possessed either of exceedingly disagreeable qualities or of very energetic natures, such as emetics, cathartics, anthelmintics, vesicants, or bitter tonics. Thus Barton indicates his self-satisfaction with, or at least his subjection to the heroic theory. In a lengthy article on phytolacca he commends its investigation because "it is certainly a plant of great activity." The fact that *Rhus radicans* produces such a terrible eruption as is the case with some people is most clearly stated by the doctor, after which he indicates where and how the decoction or the plant in substance can be used *safely,* with benefit in disease. As previously indicated, the trend of thought in those days in the medical profession was to discover substances that in action would parallel European energetic drugs. Senega is thus hopefully mentioned by Barton, as follows:

My ingenious pupil, Dr. Thomas Walmsley, has lately communicated to me an additional instance of the *salivating* power of this active vegetable.

He questions the *power* of *datura* in overcoming so virulent a disease as tetanus, as follows:

I fear that our vegetable, though by no means a *feeble* one, will be found unequal to the cure of this terrible disease.

In this sentence he unconsciously voices the transplanted idea of mediæval medicine, to the effect that *severe diseases* require *heroic treatment*.[2]

Among emetics, sanguinaria is conspicuous. The doctor believes by reason of the *acrid nature* of the *Indian turnip*, that it deserves careful investigation concerning its *promising therapeutical qualities*.

Among stimulants, the poisonous side of plants is the subject of hopefulness. For example:

I have no hesitation in referring to a number of poisonous vegetables, with the properties of which we are not so well acquainted as we ought to be. Such are the *Datura Stramonium*, or Jamestown weed, the *Cicuta maculata*, &c.

Concerning *Cicuta venenosa*, a fearful poison which kills as he states, "without inducing pain or convulsion," he adds that perhaps it is "the plant with which some of our Indians destroy themselves." He adds that it should be used with great care, concluding as follows:

I have given the powder of this plant internally in a case of fever, and have thus, at least, ascertained that it may be used with safety.

Happily, among stimulants are included a few innocuous plants, gaultheria, sassafras, spicewood, ginseng, and eryngium.

Not less energetic are the *topical stimulants*, among which, in addition to the acrid crowfoot, the cathartic butternut and a few other items are included as follows:

To this head of topical stimulants, I may refer several species of the genus *Rhus*, or *Sumac;* particularly the *Rhus radicans*, or poison vine; the *Rhus vernix*, or Vernice tree; and the *Rhus toxicodendron*, or poison oak.

[2] Let it not be forgotten that the European herbalists were not poisoners. They perhaps erred in the direction of credence in innocuous plants of no established value.

But enough for our purpose. Throughout the "Collection" we note, as has been stated, that remedial agents thought of as members of the American materia medica, and used both by the "empiricists" and the profession, partake of energetic natures or of strikingly disagreeable qualities.

Consider now the significance of what we have before us in a general application to the American materia medica. Dr. Barton was a cultured, kindly gentleman, and one of the foremost thinkers of his time. He was conspicuous as a botanist and was therefore acquainted with America's flora, being likewise hand in hand with men versed in therapy and chemistry. He was an educated man, tolerant of error and mistakes, kindly disposed towards empiricists and those engaged in domestic medication, a listener to men with information or experience records to impart, whether or not they were qualified in outside lines. He was in touch with the pioneer and the Indian, as well as adventurers who travelled in outside places, and he came into close communication with primitive men and with nature. Notwithstanding all this, we find that the "Materia Medica Americana" of Dr. Barton, known as Barton's "Collection," breathes in its every page the touch that seems to have been inherited from the spirit of mediæval European times, in which kindness to the sick and charity for the afflicted were too often exceptional. Confronting evil spirits, although not designated as devils, seemingly needed to be expelled by energetic, harsh forms of medication.

PART II.

Beginning of a Revolution.—Comes now the spirit of unrest, that, cradled during preceding years, about this date took possession of the people. There were questionings and criticisms of "authority" in medicine, that success in the great American Rebellion had perhaps made possible. Inherited methods from abroad, political or religious, were no longer accepted merely by right of inheritance or of official authority. Rebellion in politics and by arms bred rebellion in expanding thought. Inherited medicines and authoritative medication as practiced by physicians became a storm-centre of attack. European text-books, European remedies, European processes, surgical, therapeutical, pharmaceutical, came by a great part of the people to be viewed with suspicion. The rebellious populace, often illiterate and destitute of scientific education, presumed to criticize the methods as well as the practice of the medical profes-

sion. The terms *bleeders, blisterers,* and *"fashionable doctors"* were hurled against physicians of regular professional education. Empiricists, believing in domestic medication and the possibilities thereof, in contradistinction to regular medication, issued pamphlets, wrote communications to the papers, travelled about the country giving lectures and otherwise decrying the evils of the processes inherited from Europe and paralleled in America. "Better that our loved ones should be permitted to die in peace than by the torturer's hand." That cry became a battle cry.

SAMUEL THOMSON THE BOTANIC CRUSADER.—Just then came Samuel Thomson as the most pronounced of all the agitators. Dogmatic, aggressive, unflinchingly persistent, closely did he touch the people and irresistibly did he appeal to them. Throughout the country his followers and himself travelled, introducing the new "American" practice and arraigning those whom they called "fashionable doctors." The evils of bleeding, the depleting effects of violent cathartics, of blistering and of salivating were most forcibly and excoriatingly set forth. Nor could they well be exaggerated. Thomsonianism (better had it been *Thomsonism*) became a household word. Empiricism as concerns medication became the fashion with thousands. Household remedies now grew in importance, whilst home-prepared remedies were most extravagantly praised. In it all the educated physician was berated and abused without stint and without mercy. The good in his work was forgotten, the bad (and there was much bad) was never overlooked. Seizing upon the nature of the heroic remedies that were favorites Thomson and his people raised the battle cry against such methods and against such remedies. For reasons that are apparent as we look back into those days they instituted a crusade that finally succeeded. Notwithstanding the illiteracy of so many of its advocates, the rebellion against the regular profession spread like a prairie fire. The fame of Thomson and the Thomsonian remedies became established in the homes of the people throughout America, from Massachusetts to the Carolinas.

(To be concluded in February number.)

THE PHARMACOPŒIAL TESTS FOR AMMONIUM BENZOATE.*

By Atherton Seidell and George A. Menge,

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The United States Pharmacopœial description of this salt contains, in addition to the qualitative tests for ammonia, benzoic acid, and certain common impurities, only two tests which might be expected to indicate the degree of purity of the sample. These are the melting or, rather, decomposition point, and the reaction towards blue litmus paper. The following experiments show that neither of these tests is of any value in determining the purity of a given sample of the salt. The experiments we have made also show that the distillation method for ammonia determination is readily applicable to the analysis of ammonium benzoate samples and a simple adaptation of this process is therefore suggested as a quantitative method for this and similar Pharmacopœial ammonium compounds.

Analysis of Ammonium Benzoate by Distillation of the Ammonia.—The distillation method modified to the simplest conditions was found to give entirely trustworthy results. The details which were followed in the determinations reported herewith are as follows: The distillation flask was an ordinary Erlenmeyer Jena glass flask of about 350 c.c. capacity, through the stopper of which passed a plain glass tube which was bent to form an inverted U, the longer arm of which ended below the surface of the standard acid contained in the receiving flask, which was placed in an evaporating dish containing cold water. The connections which would have been required for a condenser were therefore eliminated, and the rapidity of the distillation was not appreciably affected. Tenth normal solutions were used in all cases. A convenient amount of the sample for a determination is 0.5 Gm. for which 50 c.c. of 0.1 N H_2SO_4 are to be used in the receiving flask and 50 c.c. of 0.1 N caustic alkali and about 150 c.c. of water in the distilling flask. About 150 c.c. of liquid are distilled over, and

* Presented in abstract at the meeting of the Pharmaceutical Division of the American Chemical Society, December, 1909.

the excess of acid remaining in the receiving flask titrated, after cooling, with standard ammonia solution, using cochineal as the indicator. The free alkali remaining in the distilling flask may also be determined by titration, with 0.1 N H_2SO_4 using phenolphthalein, but calculations made from this titration are subject to the error arising from the alkali dissolved from the glass of the distilling flask and also from inaccuracies of the indicator. With

TABLE I.

ANALYTICAL RESULTS OBTAINED UPON AMMONIUM BENZOATE SAMPLES BY THE DISTILLATION METHOD.

(50 c.c. 0.1 N NaOH and 50 c.c. 0.1 N H_2SO_4 used respectively in the distilling and receiving flasks for each determination.)

Sample		Distilling flask			Receiving flask			
Description	Wt. used	C.c. 0.1 N H_2SO_4 for excess NaOH	C.c. 0.1 N NaOH equivalent to C_6H_5COO	Calc. Gm. free C_6H_5COOH	C.c. 0.1 N NH_4OH for excess H_2SO_4	C.c. 0.1 N H_2SO_4 equivalent to NH_3	Calc. Gm. $C_6H_5COONH_4$	Per cent. $C_6H_5COONH_4$ found
No. 220	0.5	14.0	36.0	.006	14.5	35.5	.494	98.8
No. 220	0.5	13.9	36.1	.005	14.35	35.65	.496	99.2
No. 222	0.5	13.85	36.15	.003	14.1	35.9	.499	99.9
No. 223	0.5	13.75	36.25	.004	14.1	35.9	.499	99.9
No. 224	0.5	13.9	36.1	.003	14.15	35.85	.498	99.7
No. 220 recryst. (a)	0.5	14.0	36.0	.003	14.3	35.7	.496	99.2
No. 220 recryst. (b)	0.564	9.4	40.6	.003	9.6	40.4	.498	99.6
No. 220 recryst. (c)	0.4323	18.65	31.35	.0067	19.2	30.8	.428	99.1
No. 220 recryst. (c_1)	0.4365	13.3	31.7	.0232	20.2	29.8	.415	95.0
No. 220 recryst. (c_2)	0.4838	14.6	35.4	.0330	17.3	32.7	.455	94.0
No. 220 recryst. (c_3)	0.4186	19.35	30.65	.0494	23.4	26.6	.370	88.4
No. 220 recryst. (c_4)	0.2466	31.1	18.9	.1062	39.8	10.2	.142	57.5

In the above table the designations "recrystallized (c), (c_1), (c_2)," etc., refer to the same sample of purified ammonium benzoate, which was dried in a Hempel desiccator containing H_2SO_4 and at about 50 mm. Hg pressure for successive periods of time. These periods were respectively about 1, 2, 5, and 8 days.

samples containing large amounts of free benzoic acid, however, this latter titration serves as a useful check upon the results calculated from the ammonia determination. The character of the results which may be obtained by the method as above outlined are given in Table I.

In connection with the distillation method, it should be mentioned that on account of the low percentage of ammonia (NH_3 =

12.24 per cent.) in the compound the multiplication of the error in calculating to benzoate is considerable, and therefore the accuracy of the method is probably within only about 0.5 per cent. of the amount of the salt present. It is interesting to note that of the four commercial samples analyzed they all gave results above 99 per cent. The Pharmacopœial purity rubric of 98 per cent. for this compound might, therefore, be raised to 99 per cent. without requiring a change in the present market conditions of this product.

The Formaldehyde Method for the Analysis of Ammonium Benzoate.—This method, which depends upon the formation of hexamethylenetetramine and simultaneous liberation of the acid of any ammonium salt when an excess of a neutral solution of formaldehyde is added to it, was suggested by Schiff [1] and subsequently by Ronchèse.[2] Dr. B. Herstein, of the Drug Laboratory, Bureau of Chemistry, Department of Agriculture, recently tested this method (private communication) upon a large number of ammonium salts, including the sulphate, nitrate, phosphate, oxalate, citrate, molybdate, halogen salts, etc., and found that entirely satisfactory results were obtained.

The determination may be very conveniently made as follows: about 5 c.c. of the ordinary 40 per cent. formaldehyde is just neutralized in an Erlenmeyer flask with dilute alkali solution, using phenolphthalein as indicator, an aliquot portion of the ammonium salt solution corresponding to 0.5 Gm. is then added, and the liberated acid titrated to the first appearance of the pink color of the phenolphthalein, with 0.1 N NaOH; the solution is then heated just to the boiling point and a further amount of alkali added to the reappearance of the faint pink color. Our experiments showed that satisfactory results were not obtained when less than 3.0 c.c. or more than 10 c.c. of 40 per cent. formaldehyde were used per 0.5 Gm. of ammonium benzoate. The analytical results are given in the following Table II.

These results confirm the general conclusion that the formaldehyde method is very satisfactory for the determination of the acid radicle, and should, no doubt, be adopted as the quantitative method for most of the ammonium compounds of the Pharmacopœia. It happens, however, in the present case that, since the most common impurity of ammonium benzoate is free benzoic acid resulting from

[1] Liebig's Annalen, **319**, 75, 1901; Chem. Ztg., **27**, 14, 1903.
[2] Jour. pharm. et chim. (6), **25**, 611, 1906.

the gradual loss of ammonia, the inferiority of a given sample due to this cause is not detected as readily by the formaldehyde as by the distillation method of analysis. This fact is very forcibly illustrated by the titration of the mixture of ammonium benzoate and benzoic acid shown above. In this case, although there was present 20 per cent. of free benzoic acid, there was obtained a difference of only 1.15 c.c. (37.1–35.95) of 0.1 N NaOH from the amount theoretically required for pure ammonium benzoate. Thus, by the formaldehyde method each 0.115 c.c. of 0.1 N NaOH, when 0.5 Gm samples are employed, corresponds to 2.0 per cent. of free benzoic acid. By referring to Table I it will be found by calculation that, on the basis of the ammonia determination, the presence of 2.0

TABLE II.

ANALYTICAL RESULTS UPON AMMONIUM BENZOATE SAMPLES OBTAINED BY THE FORMALDEHYDE METHOD.

Sample No.	Gms. used	C.c. neutralized 40 per cent. formaldehyde	C.c. 0.1 NaOH required		Calc. per cent. $C_6H_5COONH_4$
			Before boiling	After boiling	
222	0.25	1.0	17.1 ?	17.65	98.2
222	0.25	3.0	17.85	17.95	99.9
224	0.50	6.0	35.45	35.95	100.0
223	0.50	8.0	35.45	35.95	100.0
220	0.50	10.0	35.55	36.05	100.3
Mixture*	0.50	6.0	36.7	37.1	103.2

* Mixture = 0.4 Gm. No. 224 + 0.1 Gm. C_6H_5COOH, *i.e.*, 20 per cent. C_6H_5COOH.

per cent. free benzoic acid is indicated by a difference of 0.74 c.c. of 0.1 N H_2SO_4 from the amount theoretically required for pure ammonium benzoate. The explanation of this advantage of the distillation over the formaldehyde method in the case of ammonium benzoate is that a given difference between the composition of two samples is a larger percentage of the ammonia than of the benzoic acid present, and therefore shows itself in nearly the ratio of the amounts of these two constituents in the compound.

Stability of Ammonium Benzoate in the Air.—Although it is stated in the Pharmacopœia that the salt gradually loses ammonia when exposed to the air, the observations which we have made indicate that such a decomposition is very slight and need not be feared with the use of ordinary precautions for protecting the sample.

Several grams of ammonium benzoate, through which a slow current of air was drawn for eighteen hours, lost an amount of ammonia corresponding to about 2 per cent. of ammonium benzoate, and it appeared that the alteration had all taken place at the point where the current of air first met the sample. Of five samples of ammonium benzoate kept in an ordinary desiccator, over H_2SO_4 for two and one-half months, four lost ammonia corresponding to about 5–8 per cent. of ammonium benzoate. The fifth, however, lost an amount corresponding to 20.7 per cent. Under diminished pressure, as might be expected, the loss of ammonia is very rapid, as will be seen by reference to the last four analyses given in Table I, and to the experiment described in connection with the melting-point determinations.

The Pharmacopœial Litmus Paper Test.—On applying this test to a number of samples containing varying per cent's of benzoic acid, it was found that even as high as 8 per cent. of the latter produced no distinct change in blue litmus paper; with samples containing 12 per cent. benzoic acid, however, the change could be detected. It is therefore apparent that the litmus paper test is valueless as an indication of the partial deterioration of ammonium benzoate within the limit stated.

Melting or Decomposition Point of Ammonium Benzoate.—The specifications under ammonium benzoate, in the Pharmacopœia, contain the following statement: "The salt fuses at 193° to 194° C. (379.4° to 381.2° F.) with decomposition . . . " Considered in connection with the purity rubric of 98 per cent., this statement would doubtless be generally construed to mean that if a sample of ammonium benzoate fuses with decomposition at 193° to 194° C., it may be considered to be 98 per cent. pure or very nearly so. Upon this assumption and in connection with an investigation now being conducted in this laboratory upon the melting points of Pharmacopœial compounds, the decomposition point of four samples of ammonium benzoate had been determined, with results that were practically concordant for the different samples and with the U.S.P. requirement, thereby indicating a purity of at least 98 per cent., which subsequent analyses confirmed. The analytical data for the different samples, however, showed a variation as great as 1 per cent., with no corresponding variation of the decomposition point. Another sample which had been kept in a vacuum desiccator for a short time and was found upon analysis to contain only 94

per cent. of ammonium benzoate, also showed a decomposition point practically identical with that of the pure material. These results led us to a more extended and systematic investigation of the effect of the presence of benzoic acid upon the decomposition point of ammonium benzoate.

Since benzoic acid is the impurity which results when ammonium benzoate is partially decomposed, we approached the problem from the two extremes of ammonium benzoate and benzoic acid, obtaining two series of samples which gradually approached each other in composition. The first series was obtained by subjecting pure ammonium benzoate to continual desiccation in the presence of sulphuric acid in a Hempel desiccator under diminished pressure (about 50 mm.), portions being removed at irregular intervals for analytical and melting-point determinations. In this way we obtained six samples, varying in composition from 98.6 per cent. to 57.5 per cent. ammonium benzoate. The last sample (57.5 per cent.) exhausted the supply of material we started with in that experiment. The second series was obtained by mechanically mixing benzoic acid and ammonium benzoate in proportions varying from 50 per cent. each at the one extreme to pure benzoic acid at the other, six samples being prepared in this way.

The melting or decomposition points determined for the different samples of both series, together with the duration of desiccation required to produce the varying degrees of decomposition indicated in the first series, will be found in the following table. The samples of the first series have been designated by Roman numerals and those of the second by letters. The method used for determining the melting points is one recently adopted in this laboratory, according to which the material, within certain limits, is heated at a definite rate (3° per minute within 20° or 25° of the melting point). A standard thermometer was used and the observed reading was corrected for emergent stem.

It would seem to require only casual consideration of the tabulated data to lead to the very definite conclusion that the decomposition point of ammonium benzoate is quite useless as a test of purity—at least, in the presence of benzoic acid, even to the extent of nearly 50 per cent.—and that, therefore, the statement previously quoted from the Pharmacopœia relative thereto should either be modified so as to insure against misinterpretation or should be omitted. The melting-point results of the mixtures shown in

Table III are perhaps more clearly exhibited by the following graphic representation. The lower curve shows the temperatures at which the various mixtures began to melt—the beginning of the melting being understood as that point at which the sample collapses or sinks down in the capillary, or that point at which the first definite trace of liquid can be detected. The upper curve repre-

TABLE III.

MELTING POINTS OF MIXTURES OF AMMONIUM BENZOATE AND BENZOIC ACID

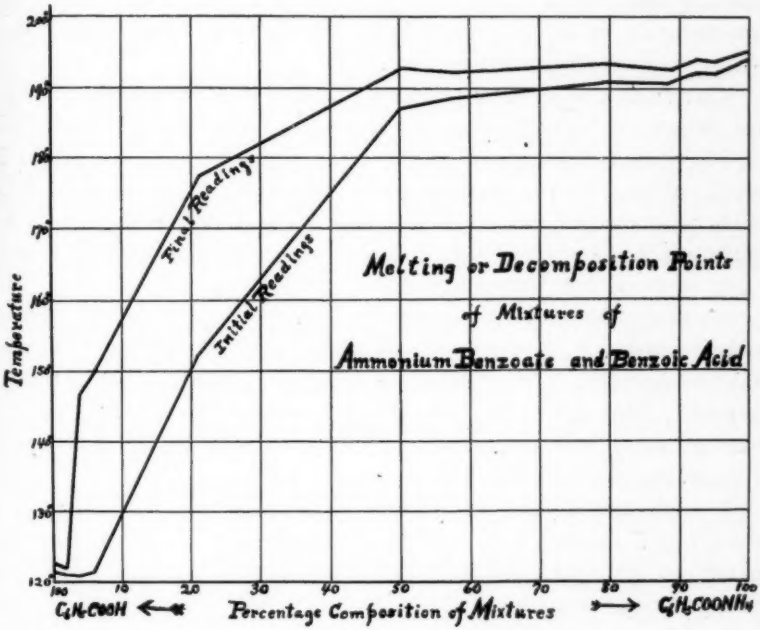
Sample	Per cent. composition		Melting or decomposition point (cor.)	Remarks
	$C_6H_5COONH_4$	C_6H_5COOH		
I	99.2	Trace	192.5° to 194.3°	Vigorous effervescence.
I_a	99.2	Trace	188.2° to 189.2°	Effervescence after 5 to 7 min.
II	99.6	Trace	193.° to 194.3°	Vigorous effervescence.
III	99.9	Trace	193.1° to 194.8°	Vigorous effervescence.
IV	99.7	Trace	193.8° to 194.8°	Vigorous effervescence.
V*	98.6	1.2	193.1° to 194.3°	Vigorous effervescence.
VI*	94.	6.4	191.7° to 193.5°	Vigorous effervescence.
VII*	92.1	8±	192.9° to 194.°	Vigorous effervescence.
VIII*	88.4	11.8	190.4° to 192.4°	Effervescence.
IX*	79.29	20.5±	190.7° to 193.3°	Slight melting and effervescence.
X*	57.5	43.	188.6° to 192.2°	Last trace effervesces slightly.
A	49.83	50.17	187.1° to 192.7°	Slight effervescence finally.
A_1	49.83	50.17	183.9° to 190.2°	Heated very slowly from 175.
B	21.	79.	152.° to 177.7°	Definite sign at 120–121 but no liquid until 152; no effervescence.
C	5.73	94.27	121.3° to 122.3° to 148.9°	Most melts 121–2; no effervescence.
C	5.73	94.27	121.3° to 131.5° to 149.°	C remelted after cooling.
D	3.85	96.15	120.8° to 121.3° to 146.9°	Behavior similar to C.
E	2.2	97.8	121.3° to 121.8°	Melts without decomposition.
F	....	100.0	121.4° to 122.4°	Melts without decomposition.

* Samples VII and IX represent degree of decomposition of two samples of ammonium benzoate as a result of standing in an ordinary desiccator over sulphuric acid for about 2½ months. Samples V, VI, VIII, and X were obtained by subjecting a sample of pure ammonium benzoate to vacuum desiccation (about 50 mm. Hg), in the presence of sulphuric acid for 6, 42, 112, and 184 hours respectively.

sents the final reading—not necessarily the point of complete liquefaction, for in all cases where 80 per cent. or more ammonium benzoate was present the effervescence was sufficiently vigorous to drive the material up the tube and in those cases the final reading represents the point of vigorous effervescence. The distance between

the two curves at any point represents the range over which the sample was melting or decomposing (heating at the rate of 3° per minute).

The curves show clearly that the variation in melting point or decomposing point between a sample of pure ammonium benzoate and a sample containing 50 per cent. of benzoic acid is barely significant. They also offer a striking commentary upon the general conception of the melting points of binary mixtures compared to the



melting point of either constituent in pure form. The almost horizontal course of the curves from 100 per cent. to 50 per cent. ammonium benzoate and the very sharp rise at 94 per cent. to 96 per cent. benzoic acid are very striking. The nature of the curves would doubtless be more or less modified by further experimentation, and perhaps by more refined methods, but for the principal purpose of this work we believe they serve just as well as they stand,—to illustrate the unavailability of the decomposition point as a test of purity.

A further indication that the decomposition point is an unreliable test for purity consists in the fact that widely varying results may

be obtained by varying the rate of heating or by holding the temperature at a given point; for example, in one experiment we were able to cause a sample of pure ammonium benzoate to decompose at 185° by holding the temperature at that point for a few minutes (I_a and A_1, Table III). The same thing has been shown to be true of other compounds which decompose on heating.

Further investigation of binary mixtures containing ammonium benzoate, also containing other compounds which decompose, will probably be conducted in this laboratory in connection with the investigation of melting points of Pharmacopœial compounds previously referred to in this article.

Conclusions.—1. The results of the simplified distillation method are shown to be sufficiently accurate for the quantitative analysis of Pharmacopœial ammonium benzoate samples. This method is better adapted to the quantitative examination of ammonium benzoate than the formaldehyde method. The latter, however, is no doubt preferable in the case of most of the remaining ammonium compounds of the Pharmacopœia.

2. The melting point or rather decomposition point of ammonium benzoate is shown to be valueless as a test for the purity of this compound. It is probable, although it cannot be stated with certainty, that with all other Pharmacopœial products having a melting point accompanied by decomposition this test for purity is, as in the case of ammonium benzoate, useless.

3. The litmus paper test is shown to be inadequate for the detection of free benzoic acid present in amounts as great as approximately 10 per cent., and is therefore misleading.

4. The Pharmacopœial description and tests for ammonium benzoate should be modified by the elimination of the litmus paper and melting-point tests, or such a qualification of the latter that will show its inapplicability as a test for purity. The quantitative estimation of the ammonia by distillation may be briefly described according to the present style of the Pharmacopœia as follows:

The ammonia from a weighed portion of about 0.5 Gm. of the sample, dissolved in H_2O, made alkaline with 50 c.c. of 0.1 N NaOH, is distilled into 50 c.c. of 0.1 N H_2SO_4 and the excess of the latter remaining after the distillation should require not more than 14.1 c.c. of 0.1 N NH_4OH, indicator cochineal.

SOME SUGGESTED STANDARDS AND CHANGES FOR THE U.S.P.

By Charles H. LaWall.

The following notes have been collected during a period of several years and embody observations made from a practical application of the various tests and requirements of the U. S. Pharmacopœia in examining a large number of substances. Some of them are not entirely new, but a number of the suggestions have not appeared in pharmaceutical literature, to the author's knowledge. They are submitted as being along the lines of constructive criticism.

Acidum Sulphurosum.—As this preparation is very prone to deteriorate rapidly, there should be a statement to the effect that the concentrated product should be assayed and diluted at the time of dispensing. This is preferable to the present official method of assay and immediate dilution and would eliminate the necessity of advising its frequent assay as given in the text.

Alcohol.—The present official method of testing for wood alcohol has been alleged to be unreliable. It would be advantageous, therefore, to substitute some authoritative method like the Riche-Bardy process of the A.A.O.A.C., as given in U. S. Department of Agriculture Bulletin No. 107.

Alumen Exsiccatum.—As recently stated by other investigators the rubric should be brought into complete accordance with practical requirements. If strictly interpreted it does not allow even a trace of moisture. This is impracticable. A limit of moisture should be given (not more than 2 or 3 per cent.) and a method for its estimation should be included.

Amylum.—Some commercial varieties of corn-starch contain appreciable amounts of nitrous acid or nitrites, which might occasion difficulty in its use as an indicator. A test for the presence of nitrous acid or nitrites by the Griess-Ilosvay method should be given.

A method for the estimation of the 95 per cent. of hydrolizable carbohydrates should also be included if this requirement is retained.

Aqua Hamamelidis.—A test for the presence of methyl alcohol should be given among the requirements for this article, as it is frequently reported as containing this substance instead of ethyl alcohol.

Aqua Hydrogenii Dioxidi.—A test for the presence of acetanilid should be given. The following is suggested:

If 100 c.c. of solution of hydrogen dioxide be shaken in a separatory funnel with chloroform, and the chloroformic layer drawn off and evaporated spontaneously to dryness, the residue, when taken up with solution of potassium hydroxide, 1 in 4, and heated in a test-tube with a few drops of chloroform, should not evolve the disagreeable odor of phenylisocyanide (isonitrile).

Elixir Ferri, Quininæ et Strychninæ Phosphatum.—A method of quantitatively estimating strychnine in the presence of quinine is needed. In case of an error, where the quantity of strychnine might be in dangerous excess, there is no method of ascertaining whether the proper ratio of the two alkaloids has been used.

Ferri Sulphas Exsiccatus.—A purity rubric should state the amount of allowable moisture, and a method for its estimation should be given.

Fluidextractum Zingiberis.—A test for the presence of capsicum is advisable. The following is suggested:

Five c.c. of fluidextract of ginger are to be heated in a shallow evaporating dish with 10 c.c. of half normal alcoholic potassium hydroxide solution and the liquid allowed to evaporate to dryness on the water-bath. The residue is then dissolved in 50 c.c. of water and transferred to a separatory funnel, 20 c.c. of ether are added, and the liquids are thoroughly mixed by agitation. If the ethereal solution be drawn off and allowed to evaporate spontaneously upon a watch glass the residue left by its evaporation should have a warm, camphoraceous taste, but no sharp pungency should be observed when the tip of the tongue is applied to the residue.

Glyceritum Ferri, Quininæ et Strychninæ Phosphatum.—As previously noted under elixir ferri, quininæ et strychninæ phosphatum.

Hydrargyrum cum Creta.—A purity rubric should be given, together with a process for estimating the amount of metallic mercury present in this preparation.

Linimentum Camphoræ.—A rubric should be included for the required percentage of camphor.

An identification test for the presence of cottonseed oil should be given, preferably Halpen's test, which gives very good results in practice.

A quantitative test for the amount of camphor should also be included. Either of the methods proposed by Prof. E. Fullerton

Cook in the N.J.P.A. Proceedings for 1905, will be found to be satisfactory. The following, taken from that source, is suggested:

A convenient quantity of camphor liniment, approximating 10 Gm., should lose not less than 20 per cent. nor more than 22 per cent. of its weight when heated upon the water-bath during twenty-four hours and weighed occasionally until a practically constant weight is reached. The following might also be included:

When observed in a 200 mm. tube in a polariscope having a sugar scale, the number of degrees observed divided by the factor 2.925 will give the percentage of camphor in the preparation.

Or this: The specific rotatory power of the sample divided by 4.694 equals the percentage of camphor in the sample.

Linimentum Chloroformi.—This preparation is one that is frequently found of deficient quality, particularly as to the amount of chloroform present. The specific gravity is an excellent criterion in this respect and a minimum figure of 1.065 at 25° C. would practically insure uniformity with the U.S.P. formula. A ready method of approximately estimating the chloroform, which is separated from the preparation by the simple addition of water, is offered by the following:

Thirty c.c. of chloroform liniment, placed in a 100 c.c. graduated cylinder and diluted to a volume of 100 c.c. by the addition of water, after thorough agitation followed by subsidence for at least one hour, should show a substratum of heavier liquid (chloroform containing some volatile oils, etc.) of not less than 9.5 c.c. at 25° C.

Liquor Chlori Compositus.—A method for the valuation of this preparation as to the amount of free chlorine should be included.

Liquor Magnesii Citratis.—Absence of magnesium sulphate should be one of the additional requirements for this preparation. The test for barium chloride in the preparation after acidulation with hydrochloric acid is satisfactory for this purpose, if a slight turbidity but no definite precipitate is the requirement. It would be still more satisfactory to follow this up with directions for making a quantitative estimation of the magnesium present and establish a rubric for the minimum amount of magnesium, expressed as magnesium pyrophosphate or calculated back to the official magnesium carbonate, although the former would be preferable. As the formula now stands, this would lead to a requirement of 4.1 Gm. of magnesium carbonate in each 100 c.c. of finished preparation or 3.56 Gm. in each 100 c.c. when expressed as magnesium pyrophosphate.

Liquor Potassii Hydroxidi.—Absence of more than traces of potassium carbonate should be insisted upon in the preparation, which undergoes a deterioration of this kind quite readily. A proper method for filtration should also be given, in consequence of the frequent necessity for removing flakes of siliceous matter which are often found floating in the liquid.

Liquor Sodii Hydroxidi.—The same suggestions made with reference to liquor potassii hydroxidi are applicable to this preparation also.

Massa Ferri Carbonatis.—A requirement for the minimum per cent. of ferrous carbonate is just as important for this preparation as for ferri carbonas saccharatus, and a similar method for its determination should be included.

A minimum limit of 40.00 per cent. Fe_2CO_3 would be satisfactory, as 41.70 per cent. is the amount theoretically present according to the formula given, and in the examination of a large number of commercial samples of this article none has ever been found to be below 40 per cent. except where it had deteriorated through age and improper keeping.

Massa Hydrargyri.—A purity rubric, together with a method for estimating the amount of metallic mercury, should be included for this preparation.

Mel.—The test for absence of cane sugar in honey is too rigid. Honey normally contains cane sugar to the extent of 7 per cent. at times.

A test for added invert sugar should be given, as commercial honey is frequently adulterated with this substance. There is one establishment, within the knowledge of the writer, making invert sugar in 4000 lb. lots for the sole purpose of adding it to honey. The added invert sugar always contains furfurol and can readily be detected by applying the aniline acetate test for furfurol, as follows:

When a mixture of aniline 1 c.c., glacial acetic acid 1 c.c., and water 2 c.c. is allowed to flow down the side of a test-tube in which several c.c. of a mixture of equal parts of honey and water have been placed, so as to form a supernatant layer, no red or pink zone should develop at the point of contact of the liquids within fifteen minutes.

Oleatum Atropinæ, Oleatum Cocainæ, Oleatum Quininæ and Oleatum Veratrinæ.—There should be processes of assay given

under each of these preparations, together with satisfactory tests for the identification of the separated alkaloid.

Oleoresina Zingiberis.—A test for capsicum should be included in the requirements for this preparation. Many commercial samples used in making ginger ale extracts contain capsicum and these occasionally find their way into the pharmaceutical trade. The method already given under fluidextractum zingiberis is satisfactory, using 1 c.c. or 1 Gm. of oleoresin of ginger in place of the 5 c.c. of fluidextract, the other quantities and the manipulation remaining the same.

Pilulæ Ferri Carbonatis.—The same requirements for a minimum percentage of ferrous carbonate are applicable here as in the case of massa ferri carbonatis, previously referred to. Theoretically 21.73 per cent. by weight of ferrous carbonate is present. Practically it never is found to be below 20 per cent. nor should a lower amount than this be permitted.

Pulvis Acetanilidi Compositus.—Methods for the estimation of the several constituents in this preparation are necessary, in view of the importance of accurately declaring acetanilid under the various laws.

Sodii Phosphas Exsiccatus.—A method for estimating the moisture usually found in commercial samples of this salt is desirable.

Spiritus Ammoniæ Aromaticus.—A minimum degree of alkalinity, preferably calculated as gaseous ammonia, would be an advantage for this preparation, which is very prone to deteriorate.

Spiritus Camphoræ.—The specific gravity of this preparation should be stated. A method for the determination of camphor should be given. The following is suggested:

Spirit of camphor should have an optical rotation of not less than + 12.2° when observed in a 100 mm. tube in a polariscope having a sugar scale. Or:

The angular rotation of spirit of camphor observed in a 100 mm. tube, when divided by .442, will give the number of grammes of camphor in each 100 c.c. of the spirit.

Spiritus Menthæ Piperitæ.—The specific gravity of this preparation should be stated. A method for the determination of alcohol should be included, and that given in the Bulletin 107, A.A.O.A.C. for flavoring extracts containing volatile oils is very satisfactory.

A method for the determination of the volatile oil is also necessary. In view of the fact that most of the published methods re-

quire the use of a centrifugal machine and special flasks, the writer made some experiments with the view of utilizing the cassia flask which is already included in the equipment necessary for applying the U.S.P. tests. The following has given excellent results,—the only disadvantage being the time required to effect separation in the absence of a centrifuge:

Twenty-five c.c. of spirit of peppermint are transferred to a cassia flask and 5 c.c. of hydrochloric acid thoroughly mixed with it. The flask is then gradually filled with warm water (70° C., 158° F.), thoroughly agitating and rotating to dislodge the globules of oil which adhere to the sides of the flask. After standing for twenty-four hours the flask is again rotated to dislodge any additional globules of oil which have collected on the sides, after which the separated volume of oil is read off. It should not show less than 2.5 c.c. of oil of peppermint by this method, corresponding to 10 per cent. by volume of oil in the preparation. This same method is applicable for the determination of oil in several of the other official spirits, such as anise, cinnamon, lavender, and spearmint.

Spiritus Frumenti.—The "Marsh" test for caramel in whiskey should sepersede the fullers earth test, which is unreliable.

Syrupus Ferri, Quininæ et Strychninæ.—A method for the separation of the quinine and strychnine, as suggested under elixir ferri, quininæ et strychninæ phosphatum, is also necessary in this preparation.

Tinctura Iodi.—A purity rubric for iodine and potassium iodide is necessary. A method for the determination of alcohol and also for the detection of wood alcohol should be given.

A method for the determination of potassium iodide is advisable. The following is suggested: 5 c.c. of tincture of iodine, evaporated on a water-bath in a tared dish, continuing the heating after subsequent additions of water until all of the iodine is volatilized and a white residue remains, should yield a residue of not less than 250 milligrammes, which should conform to the tests of identity and purity given under potassii iodidum.

Tinctura Zingiberis.—A test for the presence of capsicum is advisable. The test as given under fluidextractum zingiberis is applicable, using 10 c.c. of tincture of ginger instead of the 5 c.c. of fluidextract of ginger there directed.

MANUFACTURE OF U.S.P. CHEMICALS AND CRITICISMS OF U.S.P. TESTS FOR THE SAME.*

By George D. Rosengarten.

The Pure Food and Drugs Act of 1906, which made the U.S.P. a legal standard, naturally brought about a decided change in conditions surrounding the manufacture of U.S.P. chemicals. While the manufacturers have always desired to attain the highest purity possible for their products, it was found that it was not practicable in many instances to comply with the U.S.P. requirements. This condition, however, was largely overcome by the "Corrections and Additions" to the Pharmacopœia during 1907 and it is eminently proper to state here that the Committee of Revision gave every consideration to the mass of material that was put before them, and now, as a matter of fact, the requirements of the present Pharmacopœia, with some few exceptions, are comparatively readily attained, at least as far as chemicals are concerned.

There is, however, still ample scope for revision, and there is no question that the study of all the subjects relative to the U.S.P. and medicinal chemicals in general, owing to increased responsibilities, will be given greater attention, and the future possibilities which are open to this very interesting and broad field are of the greatest importance.

The purity rubric, which has proved to be one of the best innovations in the Pharmacopœia, gives the chemicals whenever it is possible a certain definite standard, and if in all instances the limitations of dangerous impurities are absolutely fixed by well-defined and sure tests or analyses, the presence of small quantities of innocuous substances may be permitted. Small percentages and traces of such innocuous substance, which were required to be eliminated by former Pharmacopœiæ, made the production of U.S.P. chemicals exceedingly arduous, and naturally increased the cost, which eventually had to be borne by the consumer. This can readily be understood by a simple case, taking, for example, sodium phosphate, which if made C.P. as virtually required by the U.S.P. 1890, commands a much higher price than the salt of the U.S.P. 8th Revision, which

* Read before the Scientific Section of the Philadelphia Branch of the American Pharmaceutical Association, November, 1909.

requires 99 per cent. $Na_2HPO_4 + 12H_2O$ and allows small quantities of innocuous impurities which in no way impair its therapeutic value.

However, the official description must be made so clear that there can be no question concerning poisonous and undesirable impurities, and when a chemical in question complies with the purity rubric, it certainly fulfils the Pharmacopœial requirements. A number of questions have been raised concerning this very point, and it undoubtedly was the intention of the Committee of Revision, that the purity rubric should cover the case, that when a substance is free from deleterious matters and meets the percentage required by the rubric, it complies fully with the meaning of the text.

Melting and boiling points have already been freely discussed, and there is no doubt that, as a criterion for purity of many substances, the Pharmacopœia must insist on their use for this purpose. However, it is very necessary that uniform methods should be required for their determination, and this also applies to solubilities, as experience has shown that cases have occurred where variations have been noted. Is the solubility determined by dissolving the specified quantity of the chemical in the required amount of the solvent, or is it determined by the amount of the chemical remaining in the saturated filtered mother-liquor? In the case of some alkaloids and their salts discordant results have been found, and there is evidently no question but that there should be careful revision to meet such instances.

Ash and residue determinations have been a source of considerable discussion in the laboratory. When it is stated that there should be no weighable residue, and there is no definite quantity given, it depends a great deal on the operator whether or not this requirement is fulfilled. It is also necessary in cases where evaporation is required to take the actions of the various chemicals on glass and porcelain into consideration, as the residue may be increased manifold if this necessary precaution is neglected. A platinum crucible for these determinations is not mentioned in any instance in the U.S.P., and the reason is obvious, as all of us are not in possession of such a valuable piece of apparatus, but for accurate work platinum is required. There have been instances reported of examinations of chemicals, during which porcelain crucibles were used, with the result that finally impurities were in evidence that were not present in the original substance.

The personal equation as an eminent factor goes without saying, and all lines should be drawn to cut this factor down to the smallest possible limitation of variations, so that unnecessary discussions and correspondence may be eliminated. It is necessary to have all definitions and tests made so precise that there can be no question, and the best and uniform methods should be adopted from time to time as occasion may arise, so that there may be concordant results. It is well understood, of course, that complete laboratory work cannot always be accomplished by all, but finally all the onus really comes on the manufacturer, and consequently every possible precaution is taken to protect the consumer. The productions of the laboratory are subjected to tests by chemists who have nothing to do with the manufacturing of the chemical, and, in addition, the product is not allowed to leave any department of the laboratory until the actual manufacturer is satisfied that it is correct in every particular. A record is kept of every lot, and its history may be traced from the time of its production until the time when the label bearing its particular mark is destroyed.

The question of proper apparatus for the manufacture of medicinal chemicals is sometimes very perplexing. There are at command glass, quartz, porcelain, earthenware, enamelled, metallic, and vessels of every description, but the decision as to which is best for the purpose can only be reached by long experience, and even then it is necessary to use great precaution, so that the resulting product may be of the proper purity, and it is often necessary that complex apparatus be used in order that all requirements may be met.

That all manufacturers desire that their various products coming under the head of "white chemicals" should be of the whitest is self-evident, and since the limit of iron, which is practically always present, was very much increased in the heavy metal test, it is possible to use such apparatus which otherwise would necessarily have been eliminated. Iron is almost always the cause of "off-color," but with the proper care its effects can be overcome, and even the most critical, of whom there are multitudes, can be satisfied. A more difficult proposition is the presence of mechanical impurities,—atmospheric dust, particles of carbon, milling dust, fibres from filtering and drying materials, small pieces of wood from containers, being everlasting sources of annoyance, and, in fact, it is very difficult at times to convince all that it is impracticable to manufacture material by

the ton, to mill it to a fine powder, and still obtain an absolutely clear solution.

Deterioration is another condition which arises where the natural and unavoidable change in many chemicals is concerned. Alkaloids, for instance, when subjected to light, or by age, change color yet may not lose any of their efficiency, whereas, on the other hand, such chemicals as sulphites, ammonium carbonate, etc., are undoubtedly considerably affected by such changes which occur in spite of all precautions. It is evident that the manufacturer cannot guard against such deteriorations, since they follow natural courses, but can only protect himself as far as possible by applying chemical knowledge and good common sense.

A few comments on some of the Pharmacopœia tests may be of interest:

Acetphenetidin.—To determine the presence of acetanilid, acetphenetidin is boiled with sodium hydroxide, the solution cooled, agitated with chlorinated soda solution, when a clear yellow liquid should result, and not a purplish red or brown red cloudy liquid or precipitate. Nevertheless, when making this test a precipitate is obtained, indicating the presence of acetanilid, although it could not be found by the bromine or other tests.

Acid Acetic, Glacial.—The test for empyreumatic substances is very strenuous. It is required that the tint produced by the addition of two drops of one-tenth normal potassium permanganate solution to 2 c.c. of the acid, diluted with 10 c.c. of water, should not be changed to brown within two hours. The German Pharmacopœia requires that when 5 c.c. of acid in 15 c.c. of water are mixed with 1 c.c. permanganate of potash solution (1–1000) it should not lose its red color within ten minutes.

Calcium Bromide.—If a quantity of this salt is used in testing for bromates, and only a drop of diluted sulphuric acid, a yellowish color may be developed, but in such instances bromates could not be detected by any further tests. However, if the salt is covered with diluted sulphuric acid no color results.

Calcium Phosphate.—The limit for chlorides is exceedingly difficult to attain.

Cinchonine Sulphate.—It is stated that one part is soluble in 69 parts of chloroform at 25° C., and further on there is a requirement that: "If one part of the powdered salt be macerated with frequent agitation in 80 parts of chloroform, at ordinary tempera-

tures, it should be wholly or almost wholly dissolved (limit of quinine or cinchonidine sulphate)."

Collodion.—The U.S.P. 8th Revision requires 40 Gm. gun-cotton to be dissolved in 750 c.c. ether and 250 c.c. alcohol, whereas the U.S.P. 1890 required only 30 Gm. in the same amount of solvents. The increased quantity of gun-cotton has caused some trouble where collodion is used as a base for preparations.

Glycerin.—It is apparently difficult to eliminate the last traces of butyric acid. In almost every examination of glycerin a fruity odor is noticed when treated with alcohol and sulphuric acid.

Iron Chloride Solution.—The test for oxychloride is not sufficiently exacting. It has been found that when tincture iron chloride is made from a solution which meets the oxychloride test, the tincture subsequently becomes turbid owing to an excess of oxychloride.

Lime, Sulphurated.—The test for the percentage of pure calcium sulphide is somewhat misleading, as there is always iron present, which will, on the addition of ammonia, impart a brownish color to the filtrate.

Mercury Oxide Yellow.—Criticism has been made that mercury oxide yellow contained red oxide, because it is not entirely converted into white mercuric oxalate when digested on the water-bath with oxalic acid for fifteen minutes. Experiments show that even if the yellow oxide is reduced to a very fine powder, a small portion still remains unchanged, consisting of minute lumps of a fine yellow powder, showing no crystalline appearance under a lens magnifying four diameters. This residue was not converted to oxalate even after heating for several hours. When the yellow oxide is mixed with a small quantity of red oxide, and the same test applied, the residue shows a decided red color and crystalline structure. When red oxide of mercury is powdered until it becomes the same color as yellow oxide, there is a partial conversion into oxalate at the end of fifteen minutes, but when treated with oxalic acid without powdering, there is no visible diminution of the red color at the end of two hours.

Sugar of Milk.—Even the corrected test has given considerable trouble in testing for cane sugar, and is difficult to comply with. However, when the test of the German Pharmacopœia is applied, samples which meet the other U.S.P. requirements stand the German test perfectly. This difference is occasioned by the fact that the U.S.P. requires diluted alcohol containing about 41½ per cent. by

weight, while the "Verduenter Weingeist" of the German Pharmacopœia contains 60 to 61 per cent. by weight of alcohol. In this test the sugar of milk is digested with diluted alcohol and the filtered liquid should remain clear after mixing with equal volume of absolute alcohol, and if evaporated on a water-bath there should not be a greater residue than 0.03 Gm.

From all the foregoing it would seem that further study must be given to the Pharmacopœia. While it is desirable that a high standard should be set for all medicinal chemicals, in accordance with the steady advance of modern times, yet the requirements should not be fixed on a plane beyond practical attainment, and such tests for purity as may be established should be so well proven that they will show the correct result when properly applied.

HISTORY OF MACERATION AND PERCOLATION.*

By Otto Raubenheimer, Ph.G., Brooklyn, N. Y.

In connection with this symposium held at the oldest College of Pharmacy in the U. S. it occurred to me that a historical sketch on maceration and percolation might be of interest to the members.

MACERATION.

Etymology of the word: In Latin it is maceratio, the art of soaking, derived from macero, to make soft, to soak, which again is derived from macer, lean or meagre.

This process has been in use from times immemorial.

The earliest known solvents in ancient times, besides water, were wine and wine vinegar.

Wine, as we all know, has been and is to-day used as a beverage by all nations, with the exception of the Mohammedans, being prohibited by the Koran on account of its intoxicating properties. (I am, however, informed that the Sultans drink champagne, which they do not consider as a wine.) As a medicine, wine has been and is to-day used over the entire world, and medicated wines have been employed in ancient times and continue to hold their place in the various pharmacopœias of the present.

* Read at the November Pharmaceutical Meeting, Philadelphia College of Pharmacy.

The most important solvent in classic times was undoubtedly vinegar, obtained through the acetic fermentation of wine. The ancients had the most extravagant ideas with regard to the solvent power of vinegar, not only upon vegetable but even upon mineral substances, as may be gathered from the concordant statements of Livy and Plutarch that Hannibal, the celebrated Carthagenic general, in his passage across the Alps, cleared the way of rocks by means of vinegar. I might also quote here the story which Pliny tells of Cleopatra, who in fulfilment of her wager to consume a million sesterces at one meal, dissolved some costly pearls in vinegar and drank the solution.[1]

The acid plant juices were assumed by the ancients to contain vinegar, and naturally medicated vinegars were prepared by maceration and are still official in the present pharmacopœias. The Father of Medicine, the Greek physician Hippocrates, in the 5th to the 4th century B.C., already prepared acetum scillæ, vinegar of squill.[2]

You will ask why did the ancients not use alcohol, the great solvent, and macerate therein the various drugs, etc.? My answer to this is, that, strange as it may seem, alcohol was unknown in ancient times. Not until about 1100 is the distillation of spirit from wine mentioned by Khalaf-Ebn-Abbâs Abul Kasan. Raimundus Lullus (1235–1315) named this spirit "Aqua Ardens," from ardere, to burn, burning water, a name still in use as the "Branntwein" of the Germans and the "fire water" of our Indians. A very important event in pharmaceutical history is, that Lullus was the *first* to prepare tinctures and quintessences by macerating the different drugs in spirit.[3]

But not until the 16th century did these preparations come into more general use through Phillipus Aureolus Paracelsus Theophrastus von Hohenheim, that much abused and envied physician-pharmacist, chemist, philosopher, and theosoph, the founder of iatro-chemistry (medical chemistry), which in contrast to alchemy opened new paths in chemistry and medicine by joining these two sciences. Paracelsus gave a tremendous impetus to the higher development of the apothecary's calling by his generous additions of chemicals as well as tinctures, essences, and quintessences to the materia medica. Before his time apothecary shops were nothing more than stores for roots, herbs, syrups, plasters, cerates, and especially confections. The service which Paracelsus rendered in instigating physicians and apothecaries to busy themselves with

chemistry, etc., was indeed a great one, and A. N. Scherer in his memoir "Theophrastus Paracelsus" (St. Petersburg, 1821) rightly says: "Pharmacy owes *everything* to Paracelsus."

In olden times the apothecary collected his own drugs, roots, herbs, flowers, etc., in the proper season, and he himself prepared his waters and spirits by distillation and his tinctures by maceration. The collection of drugs by the apothecary kept him in touch with botany and pharmacognosy and was especially very educational to the young pharmacist and is far superior to the selling of herbs, flowers, and even roots of *doubtful value* in *pressed packages,* as practiced by the average druggist of to-day. The old apothecary carried on this maceration in glass bottles or jars in the front window of his shop, so that the sun would strike and thereby warm the preparations. The resulting different colored tinctures very correctly can be styled as giving origin to the colored show bottles in our windows to-day.

I beg to remind the users and advocaters of maceration that agitation must not be forgotten, and I know as a fact that it is very often forgotten in this process. For obvious reasons frequent agitation, at least once a day, is essential. It might be of interest to learn that the second edition of the Netherland Pharmacopœia 1871, in the preparation of its tinctures even ordered *continual* agitation ("agitatio continua") for *7 to 28 days!* If our admirers of this so-called *simple* and *labor-saving* maceration would have to practice the Dutch method, then I believe they would soon reach a different conclusion.

Expression must necessarily go hand in hand with maceration, especially in the case of bulky drugs, as f. i. arnica flowers, in order to remove the liquid from the marc as much as possible. This, however, can never be accomplished entirely, and the retention of *strong* menstruum in the marc and the resulting indefinite finished preparation are the chief objections to the process of maceration. To overcome these, several pharmacopœias, the Hungarian, the Rumanian, the British, and the U. S., order the expressed marc to be remacerated with menstruum and then to be expressed again so as also to obtain a definite quantity of the finished preparation, as f. i. in Tinctura Arnicæ U.S.P. VIII. As the resulting liquid will be very turbid it must, last of all, be filtered. So you can readily see that the so-called simple process of maceration consists of maceration, agitation, expression, remaceration, and filtration, not so simple after all.

The *disadvantages of maceration* can be briefly summed up as follows: (1) the shaking; (2) the expressing and filtering; (3) the retention of strong menstruum in the marc and the indefinite finished product. The *advantages of maceration* are said to be: (1) the drug does not have to be a fine and uniform powder; (2) the process requires less skill and care in the manipulation than percolation; (3) there is less loss of alcoholic menstruum than by percolation.

Before leaving the subject of maceration I will say a few words about digestion, not Cleopatra's digestion, as cited before, but *pharmaceutical* digestion. Latin: digestio, derived from digerere, to distribute, which is a maceration carried on at a higher degree of temperature. Some of the pharmacopœias specify the temperature as:

	Ph. Ned. IV	Ph. Aust. VIII	U.S.P. VIII
Maceration	15°–25°	not over 20°	15°–20° in a shady place.
Digestion	35°–45°	not over 50°	
Infusion	90°–98°		

If a higher temperature is employed, as in the case of Warburg's tincture N.F. III (65°), it is best to attach an upright or reflux condenser or simply a glass tube about 4–6 feet long, so as to prevent the loss of alcohol.

PERCOLATION.

Etymology: per, through, and colare, strain.

A vast volume of literature exists on this interesting subject, and the brightest minds of all nations have spent a "lifetime of labor" in trying to perfect percolation and to enlighten us. Among these the following deserve special mentioning: Boullay, Robiquet, Guillermond, Pelletier, Pelouze, and Soubeiran of France, where percolation is said to have been originated, which, however, I find to be fallacious; Redwood, Proctor, Maben, and Ince, of Great Britain; Dieterich, Geiger, and Marpmann, of Germany; Duhamel, Procter, Parrish, Grahame, Squibb, Diehl, Oldberg, Lloyd, and Remington, in the United States. The American Pharmaceutical Association and the Philadelphia College of Pharmacy are to be congratulated upon the many faithful workers, whose contributions on percolation have been published in the Proceedings of the A.Ph.A. and first of all in the AMERICAN JOURNAL OF PHARMACY.

The oldest forerunner of percolation was undoubtedly the *lixiviation* (from lix, ash) of the ashes of plants. Aristotle, of Athens,

384–322 B.C., the celebrated Greek philosopher and founder of the peripatetic school, already described this process of obtaining crude potash. According to the plants used the resulting salt—Sal lixivius—was named as Sal absinthii, Sal cardui benedicti, etc. Lixiviation or leeching (German-Auslaugen) has been extensively practiced in various technical industries ever since. Even to-day the new Spanish and French pharmacopœias give the percolation process the name lixiviation and the French Codex devotes two and a half pages (383–385) under the title "Lixiviation."

In 1746 Comte Claude-Toussaint-Murot de la Garaye (1675–1755) published a work in Paris: "Chymie hydraulique pour extraire les sels des végétaux, animaux et minéraux par moyen de l'eau pure," in which he advocated and described the extraction of *powdered* vegetable drugs, etc., with water. "Sel" was not merely the name for a chemical salt but also for an extract or active principle, as can be seen by the old synonym "Sal essentiale tartari" which stands for tartaric acid. One of the products of the chemical and pharmacological studies and researches of this French physician and philanthropist was the preparation of the so-called "Sal essentiale de la Garaye," which was a dry cinchona extract.[4] But already in 1672 the German "Chymicus," Joel Langelot or, as it was customary those days, Latinized to "Langelottius," the alchemist and Court physician to the Duke of Schleswig-Holstein, recommended the very same method and also constructed a "philosophical mill" described by Joh. Christ Wiegleb, Geschichte des Wachstums und der Erfindungen in der Chemie (Berlin and Stettin, 1791–1792). This is by rights the forerunner of the method of displacement.

Benjamin Thompson, Count of Rumford, a born American (at Rumford now Concord, N. H.), who deserves special credit for being the first to ascertain that liquids can be boiled by means of steam, used a method of preparing coffee, resembling our present percolation, which he described in his 18th essay in *Repertory of Arts,* April and May, 1813.

In 1817 C. Johnson applied this principle to the extraction of cinchona bark in England, saying: "The machine I use is similar to the one made several years ago by Edmund Loyd & Co., 178 Strand, London, and does not differ essentially from any of those described by Count Rumford. In the Lancaster public dispensary this method is found to yield a better preparation than was formerly obtained from twice the quantity of cinchona bark" (*Annals of Philosophy,* ix, p. 451).

In 1816 the French Count Réal invented a hydrostatic extraction press or pressure percolator in which the drug is held in place by perforated disks and the solvent, contained in a tube twelve feet high, is forced through by its own pressure. Réal's process and apparatus are described in *Annalen der Pharmacie,* vol. xv, p. 80, also in Buchner's *Repertorium* and in Soubeiran's *Traité de Pharmacie,* the German translation by Schoedler which I have here for your inspection devoting seven pages (pp. 123–129) to this subject. On pages 127 and 128 the fineness of the powder and the method of packing are described by Soubeiran and the German pharmacist Geiger. Philip Lorenz Geiger, the discoverer of a number of alkaloids, as coniine, atropine, hyoscyamine, aconitine, and colchicine, also wrote a little book, *Réal's Aufloesungspresse,* Heidelberg, 1817.

A very important point in Réal's process is that he recommended to macerate the ground drug with 50 per cent. menstruum for several hours before packing it in the apparatus. No doubt the Réal process smoothed the way for the coming percolation method.

In 1834 the French pharmacist Theophile Jules Pelouze employed the process of displacement in his laboratory by extracting nutgalls in the preparation of tannic acid.

In 1835 the French pharmacist Boullay and son (the father discovered picrotoxin in 1818) published in the *Journal de Pharmacie,* vol. 21, pp. 1–22, their paper: "Considerations nouvelles sur la méthode de déplacement,"[5] giving the experience of Soubeiran, Limonin, Boudet, Buchner, Dublanc, Pelletier, and Pelouze. In the same journal, p. 113, Robiguet criticizes Boullay's claims to priority, having used the méthode de déplacement for five to six years in his laboratory and factory. I beg to point out that in Boullay's method the drug was put dry into the apparatus.

Dr. Fr. Schoedler, the translator of Soubeiran's *Traité de Pharmacie,* states, p. 115: "The science of pharmacy has *not* been enriched through the much praised méthode de déplacement of M. Boullay nor through the experiments of Guillermond. The principle and application of their method are the same as the Réal process, which has been in use over twenty years."

An abstract of the paper of M. A. Guillermond was reported as early as 1836 in the AMERICAN JOURNAL OF PHARMACY, vol. vii, p. 308, and I am glad to state that this JOURNAL of the Philadelphia College of Pharmacy has been the recipient of the largest portion of the literature on percolation ever since.

In 1838 the Philadelphia pharmacist, Augustine Duhamel, published in the A.J.Ph., vol. x, pp. 1–17, an essay, "Boullay's Filter and System of Displacement with Observations drawn from Experience." Duhamel deserves special credit, as he was the first to present this subject to the American pharmaceutical profession.

In 1839 A. Duhamel and Wm. Procter, Jr., published in the A.J.Ph., vol. xi, pp. 189–201: "Observations on the Method of Displacement," in which paper they state that in France this method is extensively applied and was *made official* in the *Codex 1835,* but in the U. S. it is hardly known, much less applied, and they make a plea for its introduction into the next U.S.P. And it was introduced into the U.S.P. 1840, which authority states in the preface: "As to the *kind of filtration* commonly *called displacement,* it is strongly recommended to those who have not made themselves practically familiar with the various sources of error in the matter of displacement to postpone its application whenever an alternative is given in this work, until they shall have acquired the requisite skill."

In 1840 this process was also sanctioned by the Edinburgh Pharmacopœia, which states: "A much superior method has been introduced which answers well for most tinctures—namely the *method* of *displacement by percolation.*" This is the first mentioning of percolation, which word is used instead of displacement. Quite a dispute arose which pharmacopœia adopted percolation first. As a matter of fact it was made official in both pharmacopœias in their edition of 1840, but the U.S.P. 1840 did not appear until 1843 and the Edinburgh Pharmacopœia 1840 was published in 1839.

As we have seen before Réal moistened the ground drug with half its weight of menstruum, Boullay used the dry powder, and the Edinburgh Pharmacopœia moistened it sufficiently with menstruum to form a thick pulp.

The British Pharmacopœia of 1864 in which percolation was introduced gives the following, according to Ince *very unsatisfactory,* general directions: "Macerate for forty-eight hours in three-quarters of the spirit in a closed vessel, agitating occasionally; then transfer to percolator and when fluid ceases to pass, continue the percolation with the remainder of the spirit." Such an authority as Ince criticizes this method as *unnecessary, wasteful,* and *messy.* As this combination method is even used to-day by some druggists, I hope they will consider these criticisms and discard this process in favor of the up-to-date percolation method.

Before the A.Ph.A., in 1858, Prof. Israel G. Grahame read an excellent paper: "The Process of Percolation or Displacement, its History and Application to Pharmacy,"[6] in which he makes the following remarks which still hold good to-day: "If I have a just conception of the principle upon which it is based, it is, that the substance to be treated and the menstruum should be presented to each other under such circumstances, that *each particle of the solvent shall be fully charged with soluble matter* and *immediately displaced with another particle,* to become in its turn saturated in a like manner; and if all the conditions of the process have been properly observed, these saturated particles collect and escape from the apparatus, and contain to the fullest possible extent all that the *menstruum is capable of taking up* and *even more than could be taken up by any other means.*" Prof. Grahame, aside from suggesting the use of the funnel as a percolator, deserves credit for advocating the use of powdered drugs of regular and definite degree of fineness, as well as the proper moistening before packing it in the percolator; both of these suggestions are even now considered indispensable to successful percolation.

A committee of the A.Ph.A., consisting of E. Parrish, I. J. Grahame, and C. T. Carney, presented a report on percolation at the 1859 meeting, giving an account of the introduction of the *kind of filtration commonly called displacement* into U.S.P. 1840, its extended use in U.S.P. 1850, and a proposed general description of *percolation* for U.S.P. 1860.[7]

Four pages (pp. 3–6) are devoted to percolation by U.S.P. 1860, "The kind of filtration known as percolation or the process of displacement," the use of a funnel being also permissible and the uniform powder being moistened with one-quarter to one-half its weight of the menstruum. In U.S.P. 1870 we find the same general description (pp. 3–6), with the exception that the powder is to be moistened with a *specified quantity* of the menstruum. In U.S.P. 1880 and 1890 this chapter has been improved by giving more explicit directions, by passing the moistened powder through a sieve, by the attachment of a long rubber tube to the percolator to regulate the flow, by directions to percolate the dregs of a tincture, and by authorizing repercolation in the preparation of fluidextracts. In U.S.P. VIII this chapter has been further improved by dividing it into distinct paragraphs, as percolators, the process, repercolation, rate of flow, and maceration, stating under the latter that percolation

is not suitable for exhausting some drugs and that the process of maceration is employed for some of the tinctures as aloes, asafetida, sweet orange peel, etc.

U.S.P. VIII has made a number of improvements in the manipulation of the percolation process. The quantity of menstruum to moisten the drug has been reduced, f. i. tinct. hydrastis: U.S.P. 1890 used 150 c.c., and U.S.P. VIII only 60 c.c.; tinct. cinchon co. U.S.P. 1890 used 200 c.c., and U.S.P. VIII only 80 c.c. Furthermore the U.S.P. 1890 directed to macerate the moistened drug for twenty-four hours and then pack it in the percolator and proceed with percolation. The U.S.P. VIII has made a great improvement in the macero-percolation process by directing to transfer the moistened drug to the percolator and, without pressing, allow it to stand, well covered, for six or in some cases twelve hours, then pack it firmly, pour on the menstruum, and when the liquid begins to drop close the lower orifice and macerate again from twenty-four to forty-eight hours and then allow the percolation to proceed slowly, in the case of tinctures from eight to fifteen drops per minute. This rate of flow in the new Swiss Pharmacopœia is twenty drops per minute, in the new Austrian Pharmacopœia thirty drops, and in the German Pharmacopœia (under extracta fluida) forty drops per minute. The new French Codex states that the twenty-four hours' percolate should weigh about one and a half times the amount of drug employed.

The fruitful work which Dr. E. R. Squibb has done as to percolation requires no further comment.

Repercolation or fractional percolation as called by Prof. Diehl was introduced by Squibb in 1866 with the object of saving alcoholic menstruum and to prepare strong solutions, as fluidextracts, without the application of heat. The origin of fluidextracts is generally credited to American pharmacy, and the work of Grahame,[8] Procter,[9] Squibb,[10] and others is well known. The U.S.P. 1850 recognized seven fluidextracts, 1860, twenty-five, 1870, forty-six, 1880, seventy-nine, 1890, eighty-eight, and U.S.P. VIII, eighty-five, now under the official title "Fluidextractum." Besides this, fluidextracts have become official in almost all pharmacopœias and are recognized as "liquid extracts" in the British Pharmacopœia.

Percolation is also gradually but steadily replacing maceration in the foreign pharmacopœias. Chapters on percolation, similar to the U.S.P. process, are adopted in these books and general formulas

for fluidextracts and tinctures are given. The greatest victory, however, which percolation has gained is its recognition by the Brussels International Conference for the Unification of Pharmacopœial Formulæ for Potent Medicaments, a copy of which can be found in that excellent "Digest of Comments on U.S.P.", Bulletin No. 49, Hygienic Laboratory, by Murray Galt Motter and Martin I. Wilbert, pp. 64–68. Article 2, b, of the Protocol states: "Tinctures of potent drugs shall be prepared of the strength of 10 per cent. and by *percolation.*" September 20, 1902, the day on which this agreement was signed, will be a memorable one in the annals of pharmacy—it marks the advent of a new era, the attainment of attempts covering nearly fifty years to unify the formulæ for potent medicaments throughout the world. It might be of interest to learn that when this Protocol was signed again by the duly authorized representatives of the various governments on November 29, 1906, at the Belgian ministry for foreign affairs, the Swedish government formulated the following reservation: "As the preparation of tinctures of drugs by percolation involves an increase in the price of these products, this method seems not altogether suitable for employment in a general manner in Sweden."

In connection with this subject it might be of interest to learn that the new Austrian and Swiss Pharmacopœias order tincture of opium to be prepared by maceration instead of percolation, the latter authority calling attention to this in a footnote. The new French Codex, by the way, orders this tincture to be prepared by dissolving 5 Gm. of extract of opium in 95 Gm. of 70 per cent. alcohol. Our U.S.P. VIII seems to have solved this problem in an excellent manner, by first extracting the opium with boiling water, then macerating in diluted alcohol, and lastly percolating.

In summing up I want to say that the disadvantages of maceration, *i.e.*, the shaking, expressing, and filtering, the retention of strong menstruum in the marc, and the indefinite quantity and strength of the finished product, are the principal advantages of percolation. The advantages of maceration are very little indeed. The uniform fineness of the ground drug used in percolation can be easily regulated by the sieve. The necessary skill and care in the manipulation of the percolation will certainly be acquired by the college teaching and principally by the practical experience, and I beg to remind you that the clerk who cannot conduct percolation properly ought not to be employed. As to the increased loss of alcoholic

menstruum by percolation, being left in the marc, the same can be expressed, distilled, or displaced by water.

In my experience the percolation process, and especially the improved macero-percolation method of our U.S.P. VIII, although the same cannot be used for the exhaustion of all drugs, decreases the labor and saves time and is a scientific method par excellence. When properly carried on all the advantages of maceration are obtained and furthermore it is superior to maceration, inasmuch as no strong menstruum is retained in the marc.

In conclusion I want to state that, although percolation has been originated in a foreign country, American pharmacists have greatly perfected this process and American pharmacy can justly be proud of it.

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MAHLON N. KLINE.

Mahlon N. Kline, President of the Smith, Kline & French Co., wholesale druggists, Philadelphia, died suddenly of heart failure on Saturday evening, November 27, while attending a meeting of the Brotherhood of St. Andrew at the Church of the Saviour, Philadelphia. Mr. Kline was so long and so intimately associated with the drug trade, both wholesale and retail, and did such excellent work in connection with drug and pharmaceutical matters that his death will be felt as a distinct loss to the industry.

Of all his other affiliations it may truly be said that none were of more deep concern to him that his relations with the Philadelphia College of Pharmacy, and his work as a member and officer reflects credit alike on his ability and loyalty to its interests. He was elected an active member in 1886 and a member of its Board of Trustees in 1897, of which latter body he became Chairman in 1901. He was elected First Vice-president of the College in 1905,

and at the time of his death was also Chairman of the committees on legislation and finance of the College, besides holding other minor offices. Mr. Kline's interest in the College was also manifested in other ways. Since 1897 he had offered an annual prize of a prescription balance to the student passing the best examination in the theory and practice of pharmacy. He was liberal in contributing to the financial support of the College, and probably his most notable contribution was as a member of the Smith, Kline & French Co. in conjunction with Mr. Howard B. French in purchasing and donating the Martindale Herbarium, in 1894.

Mr. Kline was born February 6, 1846, near Hamburg, Berks County, Pennsylvania, and was educated in the public schools. In 1865 he went to Philadelphia and laid the foundation of his successful business career in the employ of the wholesale drug house of Smith & Shoemaker. His merit was quickly recognized and three years later he was admitted to partnership in the firm.

Mr. Shoemaker retired in 1869 and the name of the firm was changed to Smith, Kline & Co., which in 1888 was incorporated under the style of The Smith & Kline Co. In 1891 a wholesale drug business of French, Richards & Co. was liquidated and Harry B. French of this firm joined the Smith & Kline Co., as its Vice-president, the name being again changed to Smith, Kline & French Co.

Mr. Kline joined the National Wholesale Druggists' Association at the time of its formation in 1882 and in 1885 was elected its President. For ten years, from 1887 to 1897, Mr. Kline served conspicuously and efficiently as the Chairman of the Committee on Proprietary Goods, which he relinquished to assume the chairmanship of the Committee on Suits against members of the association. In this connection he had proved himself invaluable in shaping the course which was pursued in the "Park" suits and in the litigation which ultimately led to the "Indianapolis Decree." In 1898 at the annual meeting of the association held in St. Louis that year, he was made Chairman of the Legislative Committee, which position with but one year's interruption he retained up to the time of his death. While acting as Chairman of the Legislative Committee Mr. Kline was largely responsible for the passage of the denatured alcohol bill and it was through his efforts largely that the law permitting of the drawback allowance on grain alcohol for export when used in medicinal and

toilet preparations or by itself was passed. He was also largely instrumental in persuading the Commissioner of Internal Revenue to allow manufacturing druggists a free use of fortified sweet wines in compounding their preparations.

He was a staunch advocate of the Pure Food and Drugs Act and devoted much effort towards bringing about uniformity of State law to conform with it.

Mr. Kline always took an active interest in the affairs of the city of Philadelphia and was foremost in many of the municipal reform matters. He was a prominent member of the Trade League of Philadelphia, which afterward became the Philadelphia Chamber of Commerce, and he likewise served on the Executive Committee of the National Chamber of Commerce instituted by Secretary Straus.

Always alive to the interest of his retail friends of the drug trade, Mr. Kline was an active member of the Pennsylvania Pharmaceutical Association and had he lived would have represented that organization at the Pharmacopœial Convention to be held next May.

Mr. Kline was a devoted member of the Church of the Saviour from which he was buried on November 30. The funeral was largely attended and among those present besides the officers, members of the Board of Trustees, and faculty of the Philadelphia College of Pharmacy, was a substantial delegation from the National Wholesale Druggists' Association and various pharmaceutical organizations with which he was identified. In connection with his church affiliations Mr. Kline was the Philadelphia leader of the Brotherhood of St. Andrew.

Mr. Kline is survived by a widow, two daughters, Mrs. Harry F. Valentine and Mrs. T. Carrick Jordan, and one son, Clarence M. Kline.

PHILADELPHIA COLLEGE OF PHARMACY.

A special meeting of the members of the Philadelphia College of Pharmacy was held December 10 to take action on the death of Mahlon N. Kline, First Vice-President and Chairman of the Board of Trustees.

The President read the call for the meeting which had been signed by seventeen members of the College and of the Board of

Trustees. He then said that in the death of Mr. Kline the College had lost one of its most able and energetic members; and as an officer the College had lost the services of a man hard to replace. He was a strong man, energetic, ready to assume any responsibility, and ready to work in any and all lines of duty. Personally his loss was a sad blow to him. The circumstance connected with his sudden death was a severe shock to him as he had been in consultation with Mr. Kline about College matters up to within four hours before his death. On this occasion Mr. Kline had advised him to take care of his health by taking a rest from business cares. His concern for others was a characteristic feature.

Communications were read from Professor L. E. Sayre, Mr. Frank G. Ryan, and Mr. C. Carroll Meyer, and a telegram from Mr. Wallace Procter, expressive of their appreciation of Mr. Kline and regret at his death.

In response to the call of the President for remarks a number of the members responded, as follows:

Dr. A. W. Miller stated that his acquaintance with Mr. Kline probably extended further back than most of those present. Their business relations brought them together almost daily for many years past, and Dr. Miller said that he always admired Mr. Kline's behavior in business affairs. He occupied a leading position in all the associations in the drug trade with which he was connected. Much of his energy was directed towards the legal questions concerning the trade. He had a singular aptitude in handling these questions and was of great service in all organizations with which he was connected. He had the highest feeling of respect for Mr. Kline, and his sudden death was a severe shock as it brought vividly to mind the uncertainty of life and the certainty of death, and as such a life should ever be kept in mind, he suggested that steps be taken to procure a portrait of Mr. Kline that should be displayed on the walls of the College.

Professor Joseph P. Remington, after referring to the illness of Mr. Kline, said:

"The almost tragic death of this noble man, occurring as it did in the church which he loved so well, while shocking to his family and friends possessed an appropriateness which develops in the mind after some time has elapsed for reflection. Mahlon N. Kline was a marvel for energy and ability, with a capacity for long persistence in grinding labor. He never shirked responsibility, and although

probably the majority of his tasks were distasteful to him, and in committee work others might leave him to bear the burden alone, he would simply gird on his armor and do the work; this was not due to an overweening opinion of his abilities, but, having grasped the handles of the plow and satisfied that the labor was honorable and for the betterment of his fellows. He would not allow difficulties to daunt him, nor obstacles to stand in his way, but with his great experience and knowledge of men he would find a way where the less able or courageous man would succumb.

"One of his favorite expressions was, 'I had no business whatever to go into this, but nobody else seems to care to push this so I must go on with it.' He frequently sought advice from those whom he believed could throw light on the problems in which he was engaged, and when discussing suggestions his quick grasp of possibilities was one of the prominent characteristics of his mind.

"His conscientiousness was a marked trait: if he had received a thought or suggestion which seemed to him valuable it was not his habit to appropriate it as his own, but he was glad to give credit to whom credit was due, and if he made a mistake or committed an error in judgment he seemed to take a delight in saying, 'I at one time thought thus and so, but I know better now.'

"Service was the keynote of his life. He had the power of directing others and gathering around him subordinates, but, at the same time, he loved detail, for he realized that many a great work would be ruined by neglect of some important detail which might seem trifling to the inexperienced but was really the key of the situation. He never thought much of his ability to speak and yet his friends, without exception, were glad to have him on their side. As a speaker he was convincing, relying upon righteousness of the cause which he was advocating and believing that all that was necessary to do to win was to state the facts. He well knew the value of a phrase or a witty turn, and he often confused the enemy by a bright sally; his repartee was remarkable and when he and his friend Redsecker were surrounded by congenial spirits, who could appreciate the play of wit, he was at his best. His sense of humor was a saving element, and the relief which it gave him when harassed by carking cares was most effective; but now that he is gone the memory of the great work that he has done in uplifting pharmacy, and his great work in moulding and influencing legislation, his quickness to detect defects in laws bearing upon pharmacy,

and his great influence with legislators made him a power for good, and it will be impossible for any one to take his place in this line of work.

"His religious life was characterized by a simplicity in devotion which was most remarkable. Caring little for the applause of men, a large part of his work was given to quiet deeds of charity and service. Whether it was a man besotted with drink at the Galilee Mission, a little child in his Sunday-school, an aged woman tottering to the grave, or a young man suffering from the effects of sin, his ear was ready and his hand stretched forth to help, because the secret of his life was service to his Master."

Professor C. B. Lowe said he was glad Professor Remington had prepared this true and grateful record of Mr. Kline, whose life was so full of usefulness. In many places he would be greatly missed, especially in the Pennsylvania Pharmaceutical Association where he was a tower of strength. In connection with his friend Mr. Redsecker, it was a great treat to listen to their sallies of wit and repartee. He would also be greatly missed in the College, but more especially in church work. He was glad that Mr. Kline showed by his activities in the church that a very busy man in business affairs could also prove to his business associates and to all others that business activity need not prevent a person being active and useful in the affairs of the church.

Joseph W. England said he felt that the highest tribute he could give to Mr. Kline was that he was a strong, broad-gauged Christian gentleman, one who practised what he preached. He loved work and in fact revelled in it. He was enthusiastic in all he did and strove to make each day's work better than the previous one. He had a most keenly developed sense of honor, and this was notable in his labors in assisting to frame the Pure Food and Drug Law. Doctor Wiley had said he owed more to Mr. Kline than any one else in framing that law. His death was tragic, but he had previously said that were it not for the shock to the living he preferred a sudden death. One of his favorite hymns was "Abide with me, fast falls the eventide," and especially the last verse; and his last moments were typical of his faith in these last lines, and in this faith he had his wish.

Professor Henry Kraemer said: "While some of us knew Mr. Kline and recognized his activities in this College and in the National Wholesale Druggists' Association, I must confess I was

not prepared for the outpouring of friends to attest to his worth and to show their respect for him, as was seen at the funeral services held November 30. I could not help but feel that as I had not comprehended the magnitude of his labors and had possibly underrated his influence and efforts as attested by the large congregation on that day, possibly there are others here in our midst whose services we should more deeply appreciate and with whom we should more willingly co-operate.

"The College needs every good man it can enlist in its work and for its support. We need to work together as men who are joined in a common cause. I am sure that if we all practised more of the open and manly criticism that characterized Mr. Kline, and were ready to deal fairly and squarely with each issue as though each one were bound by ties of comradeship and friendship, our College would in the future stand on a still higher plane. It would be safe in the keeping of those who remain and those who follow. May we always have the wisdom and the will to do our work in this exemplary way."

W. A. Rumsey said that he had known Mr. Kline for a number of years, more particularly because of his work in the Church of the Saviour, of which Mr. Kline was the Accounting Warden and Superintendent of the Sunday-school. He was a great help to the Rector and when the selection of a Superintendent of the Sunday-school was to be made and Mr. Kline was selected for the position the Rector said that no better choice could be made. The church will sadly miss him because he was always striving to do good to others, and the last act in his life was working and planning for the good of others.

Warren H. Poley said that Mr. Kline was too truthful a man for his own best interests. When interests conflicted between the wholesale and the retail drug trade his stand was always on the side of truth and honesty even if against his own business interests.

Edwin M. Boring said he had known Mr. Kline for over thirty years, and as he listened to the remarks that had been made his heart responded, and he wished to say that he was in full accord with all that had been said.

At this point in the proceedings Professor Remington moved that a committee of three be appointed to draft suitable resolutions and to report at the quarterly meeting of the College on December 27—seconded and agreed to.

E. Fullerton Cook said that he would like to say a few words as a representative of the young men. Mr. Kline's labors in behalf of the College House for three years were of very active interest in it and had endeared him to the young men. They felt his influence for good while there and they felt it also in the church. The life he had lived was one not so much to mourn for as lost, as it was to be glad that we had come in contact with it. Its influence was such as to make it a model for us all to pattern after.

John F. Hancock, of Baltimore, said he was very sorry he could not get in earlier but there was no train he could take that would permit him to be present at the opening of the meeting. He said that he admired Mr. Kline very much and that he had known him many years, and he had never met any man more poised and reliable. No doubt the eulogies passed on him in this meeting were by men who knew him better. He will be missed by a large circle. He was a great, a good, a useful man, fitted for every position he had been called to fill. These qualities must have been laid in his youth. He made the best use of his opportunities. All these memories should cause us to cherish him, for he was full of energy and devoted to his work. It made one feel proud to know such a man and to have been associated with him. This influence extended more and more like the ripple on the lake. He will continue to live in our memories. Mr. Kline's life connected closely with other great and good men who lived in Philadelphia. Their labors will serve to broaden and extend the work of the College as time goes on, and this will be a cherished memory with me. Others will rise to take Mr. Kline's place, but there will be no duplication of his life. Others will work on and leave to others the work that Mr. Kline and others have carried on for the best interests of pharmacy and the College.

The President in closing the meeting said that he felt that Mr. Hancock had greatly honored the College by his presence and he highly appreciated the sentiments he expressed.

C. A. WEIDEMANN, M.D.,
Recording Secretary.

DECEMBER PHARMACEUTICAL MEETING.

The regular pharmaceutical meeting of the Philadelphia College of Pharmacy was held Tuesday, December 21, with Dr. A. W. Miller, Corresponding Secretary, in the chair.

Mr. Stewardson Brown, Curator of the Botanical Section of the

Academy of Natural Sciences, Philadelphia, gave an illustrated lecture on the subject "Botanizing in the Canadian Rockies." Mr. Brown gave an interesting account of a botanizing trip made in the summer of 1908 along with a geographical exploration party. The territory explored was that near the headwaters of the Saskatchewan and Athabasca Rivers, which have their origin in the great Columbia ice-fields. Mr. Brown collected some 3500 specimens, and exhibited beautifully colored lantern slides of the most characteristic and abundant of these, such as *Salix herbacea,* a small plant consisting of three or four leaves and catkins, which is the most abundant plant above the timber line, growing at an elevation of 7000 or 8000 feet; species of primrose; species of pulsatilla, including *Pulsatilla occidentalis,* found in bloom on the edge of a snow bank; species of saxifrage, orchid, etc.

Remarks on Mr. Brown's address were made by the Chairman, and Professors Remington, Kraemer, and LaWall, the latter of whom moved a special vote of thanks to Mr. Brown, which was unanimously adopted.

A paper entitled "The Practical Application of the Twitchell Process of Fat Decomposition and Recovery of Glycerin," by W. J. Warner, of Los Angeles, Cal., was read on behalf of the author by Professor LaWall.

A resolution pertaining to pharmacopœial revision offered by M. I. Wilbert at the previous meeting and laid on the table for further consideration (AM. JOUR. PHARM., December, 1909, vol. 81, p. 593) was read by Professor Kraemer, and on motion of Professor Remington adopted as published.

Professor Kraemer spoke of the work being done by Dr. Joseph Neff, Director of the Department of Health of Philadelphia, to protect the health of the citizens, and after discussion offered the following resolution, which was adopted:

We, the members of the Philadelphia College of Pharmacy assembled at this meeting, desire to place on record a statement that the attitude taken by the Director of the Department of Public Health of Philadelphia is in accord with the principles of the members, and that we heartily endorse his efforts for the suppression of nostrums of all kinds used or advertised as being of use in the treatment of diphtheria, or other infectious diseases, and further that we also heartily endorse his efforts to enlighten the public in preventing disease and promoting the health of this community.

FLORENCE YAPLE,
Secretary *pro tem.*